II. REMARKS

Prior to the amendments made herein, claims 1 to 6 and 8 to 16 were pending. Claims 17 to 19 have been added herein. Accordingly, after the amendments made herein are entered, claims 1 to 6 and 8 to 19 will be pending.

A. Regarding the Examiner interviews (and interview summary)

Applicants' representative wishes to thank the Examiner for interviewing this case multiple times, concluding with an interview on November 3, 2005, after the Examiner had a chance to consult with a "specialist."

In the amendments and remarks made herein, Applicants are relying upon the substance of this last interview, conducted on November 3, 2005, in which the Examiner indicated the following:

1. That claims directed to "a mutant EGFR" gene would be allowable;
2. That claims directed to "a therapy that is effective to induce apoptosis or to increase the rate of apoptosis in a cell or tissue" would be acceptable in terms of written description; and
3. That claims directed to "a therapy that is effective to induce apoptosis or to increase the rate of apoptosis in a cell or tissue" would still have an issue in terms of enablement because the application shows data regarding only one such therapy, specifically, regarding cisplatin. The Examiner therefore requested data regarding another therapy.

B. Regarding the claim amendments

Claims 1, 9 and 13 have been amended herein by replacing the tem "a typrosine kinase inhibitor" with "Tyrphostin AG 1478 or its derivative." Similarly, claims 8 and 16 have been amended to recite Tyrphostin AG 1478. These amendments are supported throughout the application.

Claim 5 has been amended to correct a typo.

New claims 17 to 19 have been added and are directed to cisplatin. The new claims are supported throughout the application.

Because the amendments made herein are fully supported, no issue of new matter arises.

C. Regarding the written description rejection

Claims 1 to 6 and 8 to 16 are rejected under 35 U.S.C. §112, first paragraph, as allegedly failing to comply with the written description requirement. Applicants respectfully traverse the rejection.

1. Regarding tyrosine kinase inhibitors

The Action alleges that reciting the term "tyrosine kinase inhibitor" with correlating this function to some structure does not satisfy the written description requirement because it does not give the skilled artisan an adequate idea of the claimed genus.

Applicants strongly disagree with these allegations. "Tyrosine kinase inhibitors" cannot be defined structurally, as they have no one common structure. Rather, they can only be defined by function, and the skilled artisan would understand this "genus" by this function, as this is how (and only how!) this class is well understood. Thus, Applicants were in possession of the claimed genus at the time the subject application was filed. This is in sharp contrast to the *Eli Lily* case, where a novel gene was at issue and could have been described structurally had the inventors at issue been in proper possession of the gene.

Nevertheless, to promote prosecution of the subject application, Applicants have amended the claims by deleting this term.

2. Regarding a mutant EGFR gene

The Action alleges that only the ΔEGFR mutant is disclosed. However, the specification references other genetic rearrangements. See page 4, line 15. More importantly, as disclosed in the specification, the particular mutation to the EGFR gene is not critical to the invention. See page 12, line 20.

As stated in the Action, "[i]t is only necessary that the patent set forth enough detail to allow a person of ordinary skill in the art to understand what is claimed and to recognize that the inventor invented what is claimed." Applicants have met this standard regarding "a mutant EGFR gene." The skilled artisan would understand what is meant by this and, therefore, understand the claimed genus.

Furthermore, in an interview with the Examiner on November 3, 2005, after consulting a "specialist," the Examiner agrees that this would no longer be an issue. Therefore, claims directed to "a mutant EGFR gene" would be allowable.

3. Regarding a therapy that is effective to induce apoptosis

The Action further alleges that such therapies are only described in terms of function. However, as pointed out in the interview, such therapies can only be described by function. There is no common structure to all therapies that can induce apoptosis.

Moreover, if this were required, no generic claim directed to an apoptotic agent would ever be allowed, regardless of the depth of the disclosure in the speicification. This is not what was intended by *Eli Lily*, where a gene (a) could have been described structurally had it been properly possessed by the applicants; and (b) the genus was not properly described to the skilled artisan without such information. In complete contrast, the genus of apoptotic agents cannot possibly be described structurally. Moreover, the skilled artisan would generally understand such a genus without such information. Indeed, numerous examples of the genus are described in detail in the subject specification. See page 17, line 8.

Finally, in an interview conducted on November 3, 2005, the Examiner agreed that this would no longer be an issue for the reasons outlined above. Accordingly, Applicants respectfully request that this rejection be withdrawn.

D. Regarding the enablement rejection

Claims 1 to 6 and 8 to 16 are rejected under 35 U.S.C. §112, first paragraph, as allegedly non-enabling. Applicants respectfully traverse the rejection.

1. Regarding tyrosine kinase inhibitors

The Action alleges that the specification is enabling only for the recited agents, namely, AG1478. Applicants disagree with this allegation because the specification discloses that any tyrosine kinase inhibitor within the scope of the invention can be used.

Nevertheless, to promote prosecution of the subject application, Applicants have amended the claims by deleting this term.

2. Regarding a mutant EGFR gene

The Action alleges that only the ΔEGFR mutant is enabling. However, the specification references other genetic rearrangements. See page 4, line 15. More importantly, as disclosed in the specification, the particular mutation to the EGFR gene is not critical to the invention. See page 12, line 20. The skilled artisan would understand this and know how to use such mutants to carry out the claimed invention.

Furthermore, in an interview with the Examiner on November 3, 2005, after consulting a "specialist," the Examiner agrees that this would no longer be an issue. Therefore, claims directed to "a mutant EGFR gene" would be allowable.

3. Regarding a therapy that is effective to induce apoptosis

The Action alleges that only particular agents are enabling. More specifically, in the interview conducted on November 3, 2005, the Examiner indicated that, while cisplatin was shown to have a "synergistic" effect with AG1478, no other apoptotic agent had been shown to have such an effect. Therefore, generic claims to apoptotic therapies are not enabling because the shown synergistic effect could be related only to the particular structure or mechanism of action of cisplatin.

In response, Applicants introduce as Exhibit A Johns et al., PNAS, 100:15871-76 (2003). Johns confirms the disclosure of the subject specification, namely, that claimed apoptotic therapies go beyond cisplatin or its chemical structure. More specifically, Johns discloses that AG1478 and a completely different apoptotic agent, temozolomide, have a synergistic effect. See Abstract and entire article.

Moreover, cisplatin and temozolomide have completely different chemical structures. Further, they have different mechanisms of action. Cisplatin is thought to bind to DNA and interfere with normal transcription. See Abstract of Fuertes et al., Current Med Chem, 10:257-66 (2003), attached hereto as Exhibit B. By contrast, temozolomide is a methylating agent. See Abstract of D'Atri et al., Mol Pharm, 54:334-41 (1998), attached hereto as Exhibit C.

The additional information submitted herewith shows that the claimed invention is not limited to cisplatin, it chemical structure or its mechanism of action in inducing apoptosis. Accordingly, Applicants respectfully request that this rejection be withdrawn.

E. Regarding the anticipation rejection

Claims 1 to 4 and 9 to 15 are rejected under 35 U.S.C. § 102(b) as allegedly anticipated by Tsai et al. with Garcia de Palazzo et al. or Paez et al. to support inherency. More specifically, it is the Action's position that Garcia de Palazzo and Paez each teaches that mutant EGFR genes are expressed in many cases of lung cancer and, therefore, Tsai inherently anticipates the claimed invention. Applicants respectfully traverse the rejection.

As the Action admits, Tsai (or the other cited references) does not provide any data or disclose that AG825 is relatively selective for mutant EGFR. The Action merely assumes this from the enhanced chemosensitivity. However, this does not support a prima facie case of inherency because it does not preclude the real possibility that AG825 is also active against wild type EGFR and not relatively selective for the mutant.

Nevertheless, to promote the prosecution of the subject application, Applicants have deleted the term "tyrosine kinase inhibitor" from the claims. Accordingly, Applicants respectfully request that the rejection be withdrawn.

F. Regarding the previous Office Action

With great respect for the Examiner, Applicants would like to reiterate that in the Office Action mailed March 11, 2004, the claims as now amended were deemed to be completely allowable. On top of this, Applicants have provided herein clear evidence and additional information confirming that the claimed invention is not limited to any one apoptotic agent, structure or mechanism of action. Accordingly, Applicants would be very grateful if a Notice of Allowance is finally issued.

III. CONCLUSION

All of the issues raised in the Office Action have been addressed and are believed to have been overcome. Accordingly, it is respectfully submitted that all the claims under examination in the subject application are allowable. Therefore Applicants respectfully request a Notice of Allowance to this effect.

Respectfully submitted,

Martin D. Moynihan
Registration No. 40,338

Date: November 28, 2005

Encl.
Request for Two-month Extension of Time
Exhibits A, B, C